Povidone-iodine (PVP-I)

CAS ID: 25655-41-8 (Povidone-iodine); 9003-39-8 (Povidone); 88-12-0 (1-ethenyl-2-pyrrolidone, 1-vinyl-2-pyrrolidone); 7553-56-2 (Iodine)

Chemical formula: $(C_6H_9I_2NO)_n \cdot I_x$

Synonyms / Trade names: Polyvinylpyrrolidone-iodine, PVP-I, Argentyne, Ovadine, Iodophor, Betadine

Chemical composition: Povidone-iodine is a complex consisting of a synthetic organic polymer (povidone, also called polyvinylpyrrolidone or PVP) that serves to disperse elemental iodine into water. Povidone polymer (EPA 2006) can have molecular weights ranging between 10,000 – 1,000,000 amu (atomic mass units). The monomer used in the synthesis of povidone polymer is 1-ethenyl-2-pyrrolidone, chemical formula C_6H_9NO. Commercial povidone-iodine solutions used at fish hatcheries contain 10% dry weight iodine (range 9 – 12%) dissolved in water, in which the povidone-iodine complex is freely soluble. Povidone-iodine itself is a white solid at room temperature. Commercially available products may contain a small amount of pH buffering material, because the release of elemental iodine can result in acidification of water, as described in the environmental fate section for povidone-iodine.

Hatchery use: Primary use is as a bath treatment to disinfect fish eggs prior to hatch. The commercially available 10% povidone-iodine solution is diluted before use in disinfecting fish eggs. The diluted solution to which fish eggs are exposed contains 50 – 100 mg/L iodine. Povidone-iodine is effective against many bacterial, fungal and viral infections. A secondary, less common use is to disinfect boots and other small pieces of equipment.

Measures of Exposure:

Povidone-iodine (PVP-I) is classified as a low regulatory priority aquaculture drug by the FDA (2011). It is not used in the sections of hatchery facilities containing larval, juvenile or adult fish that discharge to surface waters. With respect to fish, PVP-I is only used to treat fish eggs during or after water hardening of the eggs, after which the solution is discarded, generally to land treatment. Exposure durations of eggs to PVP-I are short, on the order of 10 minutes (AFS 2011). Although the AFS (2011) recommended exposure duration and exposure concentration are 10 minutes at 100 mg/L available iodine for disinfection of fish eggs, the actual exposure durations and concentrations to which fish eggs are exposed, as well as disposal practices vary somewhat among Washington hatcheries.

As the use and disposal practices of PVP-I when used to disinfect small pieces of equipment or gear may also vary among hatcheries, the potential amount of PVP-I discharge from this use is unknown but likely low. Given that the conceptual site model (Figure ???) for this evaluation considers all chemicals used in baths have at least a potential to be released to surface waters, EPA has chosen to evaluate the potential for risks to ESA listed species in surface waters from exposure to PVP-I.

The remainder of this measures of exposure assessment will evaluate two aspects that combined define the exposure of ESA listed species to PVP-I in the environment: its environmental fate once released into the environment, and its expected environmental concentration.

Environmental Fate of Povidone-iodine

This section will describe the expected environmental fate of three chemicals:

1. The parent povidone-iodine complex
2. Povidone, present after it has released its complexed iodine
3. Iodine

Povidone-iodine

The parent compound used in disinfection of fish eggs, povidone-iodine (PVP-I), is a water soluble complex of a synthetic organic polymer (polyvinylpyrrolidone or PVP) which binds a number of triiodide (I_3^-) anions. Triiodide bound within the polymer is converted to free molecular iodine (I_2) and povidone polymer when a 10% solution of povidone-iodine is diluted in water. Molecular iodine is one of the two chemical forms of iodine believed responsible for the disinfecting properties of iodine. The release and conversion of the bound triiodide within povidone-iodine to molecular iodine within water is not instantaneous, but rather occurs over a period of minutes. EPA has been unable to find specific information on the reaction rate for the conversion of triiodide to molecular iodine. But considering the recommended exposure duration of fish eggs to PVP-I is 10 minutes (AFS 2011), and that diluted PVP-I solutions are only used once to treat eggs, then discarded, is evidence that the conversion of bound triiodide to free molecular iodine is essentially complete within 10 minutes.

A detailed description of the reactions of PVP-I in water is given in a review (Gottardi 2001) of the environmental fate of iodine compounds used in disinfection. Povidone-iodine (10%) diluted in water results in an increase (not a decrease as would normally be expected) in the concentration of molecular iodine in the water. The maximum molecular iodine in water concentration is reached at approximately 0.1% PVP-I in water (1000 mg/L), although the amount of molecular iodine present in a 0.01% PVP-I solution (100 mg/L, the recommended exposure concentration for disinfecting fish eggs) is not substantially lower than that in the 0.1% PVP-I dilution. Upon further dilution below 0.01% PVP-I, the amount of molecular iodine in water also begins to decrease.

Povidone

The definitive study of the environmental fate of povidone in surface water appears to be that of Trimpin et al. (2001). Trimpin et al. (2001) dissolved 10 mg/L of povidone in a fixed bed reactor, through which Rhine River water flowed for 30 days. After 30 days, no oxidation of the terminal hydroxyl groups of the polymer was observed. Nor were any changes in the repeating units of the polymer itself observed. Trimpin et al. (2001) concluded that povidone was unlikely to degrade in the environment, and further concluded that its likely ultimate environmental fate would be sorption onto solid products. The recalcitrance of povidone polymer to biodegradation was confirmed by Julinova et al. (2013), who attempted with minimal success to increase the biodegradation of povidone in wastewater treatment plants.

Because povidone does not appear to biodegrade in the environment, it appears unlikely that any of the monomer from which povidone is synthesized (1-ethenyl-2-pyrrolidone) is present in receiving waters due to degradation of PVP-I used at fish hatcheries.

Iodine

Iodine is a chemical element, atomic number 53, atomic weight 126.9. In addition to its disinfectant properties, it is also the heaviest element known to be nutritionally essential for life. Iodine is required for the synthesis of the thyroid hormones thyroxine and triiodothyronine.

As a halogen element, the chemical properties and environmental fate of iodine are similar to those of chlorine (Section ???), although apparently not as well studied as chlorine. There are at least 10 chemical forms of iodine that can be present in water, although a number of them are found at only extremely low concentrations under the circumneutral pH conditions between pH 6.5 – 9.0 of most surface waters. Molecular elemental iodine (I_2) and hydriodic acid (HOI) are the only two chemical forms of iodine believed to exhibit disinfecting properties (Gottardi 2001).

At least 10 different chemical species of iodine are present in freshwater, most of which are present to some extent at pH 6 or greater. Chemical forms of iodine known to be present in freshwater include:

$$I_2, I^-, I_3^-, I_5^-, I_6^{-2}, HOI, OI^-, HOI_2^-, OI_2^{-2}, H_2OI^+, and\ IO_3^-$$

These 10 chemical forms of iodine undergo at least nine different chemical equilibrium reactions (Gottardi 2001).

$$I_2 + H_2O \leftrightarrow HOI + I^- + H^+ \ \ (hydrolysis)$$

$$HOI \leftrightarrow OI^- + H^+ \ \ (dissociation\ of\ HOI)$$

$$I_2 + I^- \leftrightarrow I_3^- \ \ (triiodide\ formation)$$

$$HOI + H^+ \leftrightarrow H_2OI^+ \ \ (protonization\ of\ HOI)$$

$$I_3^- + I_2 \leftrightarrow I_5^- \ \ (pentaiodide\ formation)$$

$$2I_3^- \leftrightarrow I_6^{-2} \ \ (dimerization\ of\ I_3^-)$$

$$OI^- + I^- + H_2O \leftrightarrow HI_2O^- + OH^- \ \ (iodination\ of\ OI^-)$$

$$HI_2O^- \leftrightarrow I_2O^- + H^+ \ \ (dissociation\ of\ HI_2O^-)$$

$$3HOI \leftrightarrow IO_3^- + 2I^- + 3H^+ \ \ (disproportionation)$$

Elemental iodine (I_2) itself has relatively poor water solubility, with a maximum solubility of 338.3 mg/L at 25°C at pH 5 (Gottardi 2001). The water solubility of elemental iodine is greatly increased by addition of iodide anion (I^-), the basis for the well known disinfectant known as

Lugol's solution. Binding of iodine with povidone polymer provides for the release of elemental iodine at the concentration required to disinfect fish eggs during hatchery operations.

Expected Environmental Concentration (EEC) of Povidone-Iodine

The desired concentration of elemental iodine, the active ingredient used to disinfect fish eggs in trays or other egg rearing devices at hatcheries, is between 50 – 100 mg/L. Iodine constitutes, on average, 10% by weight of the total mass of povidone-iodine added to water as a disinfectant. The total concentration of povidone-iodine, which includes both the povidone polymer and elemental iodine, would therefore be in the range of 500 – 1000 mg/L. Without any dilution, this is the maximum concentration of povidone-iodine that would be found in the receiving water environment where the T&E species under evaluation are found. Based on communications with Washington hatcheries, a number of hatcheries discharge spent egg disinfecting solutions via land disposal. If spent PVP-I solutions are discharged at all to surface waters, they would first be substantially diluted before discharge.

The desired treatment concentration of iodine at all 13 Washington hatcheries that currently report its use is 100 mg/L as iodine. Since elemental iodine constitutes 10% by weight of povidone-iodine, the desired treatment concentration of povidone-iodine is 10 times the iodine treatment concentration, or 1000 mg/L PVP-I. Four of the 13 hatcheries using PVP-I have provided EPA with the annual and daily use rates, volumes, and hatchery discharge volumes necessary to calculate EECs for both PVP-I and elemental iodine. They are the Carson and Quilcene National Fish Hatcheries, the Skookum Creek Fish Hatchery and the Chief Joseph – Columbia Hatchery. This information permits us to calculate the expected environmental concentration (EEC) of both PVP-I and elemental iodine in water at the point where the hatchery discharges into a receiving water (i.e. the end of pipe chemical concentration). This end of pipe concentration is used as a conservative estimate of the chemical concentration in receiving waters prior to any dilution of hatchery discharges by the receiving body of water. This EEC calculation also does not take into account any degradation of either PVP-I or elemental iodine described in the environmental fate portion of this Measures of Exposure section.

As described in the Problem Formulation section of the methodology used in this BE, the EEC is calculated as follows, based on procedures described in Schmidt et al. (2007).

$$EEC = \frac{C \times V}{F + E}$$

Where: EEC = Expected environmental concentration (mg/L or µg/L)

C = Treatment concentration of chemical in the hatchery (mg/L or µg/L)

V = Volume of chemical used (gallons/day)

F = Volume of water discharged from hatchery to receiving water (gallons/day)

E = Effluent pond volume (gallons)

For the purposes of calculating conservative EECs, EPA has assumed that the effluent pond volume is zero. Under the lowest and highest daily hatchery discharges from the Carson, Skookum, Quilcene and Chief Joseph-Columbia hatcheries, the ranges of EECs based on their PVP-I use patterns and rates are presented in Table PVP-???, along with the calculated EEC for each of the hatchery discharge volumes.

Table PVP-???. Range of EEC values for discharge of povidone-iodine concentrations to receiving waters under lowest and highest daily hatchery discharge volumes to receiving water.

Hatchery	PVP-I Use Gallons/year	PVP-I Use Gallons/day	PVP-I Use Days/year	Discharge Gallons/day	PVP-I Treatment µg/L	EEC µg/L
Carson – low	4	0.98	4	15,399,360	1,000,000	0.064
Carson – high	4	0.98	4	39,566,800	1,000,000	0.025
Skookum – low	45	0.24	188	1,371,184	1,000,000	0.178
Skookum – high	45	0.24	188	8,732,160	1,000,000	0.028
Quilcene - low	26	0.09	289	59,305	1,000,000	1.47
Quilcene - high	26	0.09	289	31,966,747	1,000,000	0.0027
Chief Joseph - low	35	0.19	184	12,417,120	1,000,000	0.015
Chief Joseph - high	35	0.19	184	16,872,720	1,000,000	0.011

The highest and lowest EEC values from Table PVP-??? (1.47 and 0.0027 µg/L, highlighted in green) are used as the EEC range for the remaining hatcheries that did not provide the information needed to derive EECs. This range of EECs is assumed for the remaining hatcheries ~~ir~~regardless of whether their discharge is into freshwater, estuarine or marine systems. No Washington hatcheries currently have empirical data on PVP-I concentrations in their discharges to surface waters.

The EEC concentrations from Table PVP-??? will be compared to the chronic NOEC estimates calculated in the Measures of Effect section. This comparison will take place in the Risk Characterization section to estimate ecological risks to T&E species exposed to povidone-iodine discharges from hatcheries in Washington.

Expected Environmental Concentration (EEC) of Elemental Iodine

The desired concentration of elemental iodine, the active ingredient used to disinfect fish eggs in trays or other egg rearing devices at hatcheries, is between 50 – 100 mg/L. Without any dilution, this is the maximum concentration of elemental iodine that would be found in the receiving water environment where the T&E species under evaluation are found. Based on communications with Washington hatcheries, a number of hatcheries discharge spent egg disinfecting solutions via land disposal. If spent PVP-I solutions are discharged at all to surface waters, they would first be substantially diluted before discharge.

The elemental iodine EECs are calculated in the same manner as were the PVP-I EECs in the previous section, with the exception of a starting iodine concentration of 100 mg/L (= 100,000 µg/L), instead of the 1000 mg/L PVP-I initial treatment concentration. Data from the same four hatcheries (Carson, Skookum, Quilcene and Chief Joseph – Columbia) were used in the calculation of both povidone-iodine and elemental iodine EECs. Elemental iodine EECs are presented in Table PVP-?

Table PVP-?. Range of EEC values for discharge of elemental iodine concentrations to receiving waters under lowest and highest daily hatchery discharge volumes to receiving water.

Hatchery	PVP-I Use Gallons/year	PVP-I Use Gallons/day	PVP-I Use Days/year	Discharge Gallons/day	Iodine Treatment µg/L	EEC µg/L
Carson – low	4	0.98	4	15,399,360	100,000	0.0064
Carson – high	4	0.98	4	39,566,800	100,000	0.0025
Skookum – low	45	0.24	188	1,371,184	100,000	0.0178
Skookum – high	45	0.24	188	8,732,160	100,000	0.0028
Quilcene - low	26	0.09	289	59,305	100,000	0.147
Quilcene - high	26	0.09	289	31,966,747	100,000	0.00027
Chief Joseph - low	35	0.19	184	12,417,120	100,000	0.0015
Chief Joseph - high	35	0.19	184	16,872,720	100,000	0.0011

The highest and lowest EEC values from Table PVP-? (0.147 and 0.00027 µg/L, highlighted in green) are used as the iodine EEC range for the remaining hatcheries that did not provide the information needed to derive EECs. This range of iodine EECs is assumed for the remaining hatcheries ~~ir~~regardless of whether their discharge is into freshwater, estuarine or marine systems. No Washington hatcheries currently have empirical data on elemental iodine concentrations in their discharges to surface waters.

The iodine EEC concentrations from Table PVP-? will be compared to the chronic NOEC estimates calculated in the Measures of Effect section. This comparison will take place in the Risk Characterization section to estimate ecological risks to T&E species exposed to elemental iodine discharges from hatcheries in Washington.

Measures of Effect:

For fully aquatic species, the available toxicity data was identified from a search in EPA's ECOTOX database (http://cfpub.epa.gov/ecotox/). Searches were performed on the following chemical forms of povidone iodine, povidone and iodine:

- Povidone iodine, CAS ID 25655-41-8
- Povidone, CAS ID 9003-39-8
- 1-ethenyl-2-pyrrolidone, 1-vinyl-2-pyrrolidone (both with CAS ID 88-12-0)
- Iodine, CAS ID 7553-56-2
- Iodide, CAS ID 20461-54-5
- Hydriodic acid, CAS ID 10034-85-2
- Triiodide, CAS ID 14900-04-0
- Potassium iodide (most common inorganic iodide salt), CAS ID 7681-11-0

A combined total of 69 toxicity records were identified from the above search. These results are presented in Appendix ???, Table ???

- Iodine (N = 35): 7 for *Daphnia magna*, 1 for zebra mussel, 4 for bluegill, 12 for channel catfish, 1 for guppy, 10 for rainbow trout
- 1-ethenyl-2-pyrrolidone (N = 4): 4 for Red Sea bream
- Povidone iodine (N = 19): 2 for *Dunaliella euchlora*, 1 for *Pavlova lutheri*, 1 for *Phaeodactylum tricornutum*, 1 for Asiatic clam, 3 for quahog, 9 for rainbow trout, 2 for largemouth bass
- Potassium iodide (N = 11): 10 for rainbow trout, one for zebra mussel

Of the available toxicity data, the only information on a T&E species under evaluation in this BE is for rainbow trout. We have evaluated the toxicity of two different chemical forms: the parent povidone iodine, and elemental iodine (I_2). The available rainbow trout data permits us to estimate the toxicity of both povidone iodine and elemental iodine to all ESA listed salmonid species in Washington using the methodologies described under the problem formulation section of this BE, specifically using ICE models.

Toxicity of Povidone Iodine (PVP-I)

No toxicity studies meeting EPA requirements for use in developing aquatic life criteria are available for povidone iodine. Of the available data, the most useful in evaluating potential povidone iodine toxicity to T&E species in receiving waters is a chronic 35 day exposure of rainbow trout eggs and fry to the commercial povidone iodine product Betadine® (Amend 1974).

Amend (1974) exposed rainbow trout eggs from fertilization to hatch of fry using a pulsed exposure experimental design. Specifically, four weekly 15 minute exposures of fertilized rainbow trout eggs to PVP-I at a concentration of 100 mg/L elemental iodine were performed. This exposure scenario resulted in a much longer exposure time of eggs to PVP-I than is normally employed by hatcheries, and exposure of eggs at developmental stages normally not exposed to PVP-I under standard hatchery operating conditions. Amend (1974) observed no adverse effect on eggs or fry after hatching from this exposure scenario.

As Amend (1974) evaluated povidone iodine effects over a 35 day period, with exposures of longer duration than normally used at hatcheries, we consider this study to be of chronic duration. Thus, the reported 35-day chronic NOEC concentration of 100,000 µg/L povidone iodine is considered to be the chronic NOEC for steelhead under the pulsed exposure conditions in Amend (1974).

Because no empirical toxicity data for any other T&E fish species in Washington exists for povidone iodine, we used the rainbow trout chronic NOEC of 100,000 µg/L from Amend (1974) as input to the Interspecies Correlation Estimation (ICE) model to estimate toxicity to the other five T&E salmonids in Washington.

Output of all ICE models run with povidone-iodine for the T&E species, genera or family with available data in ICE is shown in Table PI-1. Using the ICE model selection guidelines set forth in the problem formulation, models used to estimate chronic NOEC's for salmonid species are highlighted in green and bolded in Table PI-1 The remaining ICE models, with poorer predictive ability and which were not selected as the source of chronic NOEC's, are shown in red in Table PI-1. As described in the problem formulation, the lower 95% confidence interval of the predicted chronic NOEC, if available, is used as the chronic NOEC in this BE. All ICE models used for povidone-iodine generated lower 95% confidence intervals of the chronic NOEC, and are shown in this section. No information is available in ICE for any of the T&E rockfish species, genera or families in Washington (bocaccio, canary rockfish, yelloweye rockfish). Therefore, PVP-I effects on rockfish cannot be quantitatively evaluated, and must be considered as an uncertainty in this BE.

The final selected chronic NOEC values for bull trout, Chinook salmon, chum salmon, coho salmon, sockeye salmon and steelhead that were compared to the expected environmental concentration of povidone-iodine in receiving water environments are summarized in Table PI-2.

Table PI-2. Chronic no effect concentrations (NOEC) for povidone-iodine

Species	Chronic NOEC (µg/L)	Source of chronic NOEC
Bull trout	52,911	ICE model – family level
Chinook salmon	41,731	ICE model – species level
Chum salmon	52,911	ICE model – family level
Coho salmon	52,911	ICE model – family level
Sockeye salmon	52,911	ICE model – family level
Steelhead	100,000	Empirical data (Amend 1974)

Toxicity of Elemental Iodine (I_2)

No toxicity studies meeting EPA requirements for use in developing aquatic life criteria are available for elemental iodine. Of the available data (Appendix ???, Table ???), the most useful in evaluating potential iodine toxicity to T&E species in receiving waters is a 96 hour LC_{50} survival study of the toxicity of three iodine chemical species (elemental iodine, iodide anion and iodate anion) stable in water to rainbow trout fry (Laverock et al. 1995). The Laverock et al. (1995) study is well designed, its two primary shortcomings are that rainbow trout were exposed to iodine under static as opposed to flow through exposure conditions, and limitations of the analytical chemistry methods for iodine.

Several 96 hour LC_{50} endpoints are available in Laverock et al. (1995), as they evaluated the effects of water hardness, total organic carbon and chloride concentrations on the toxicity of iodine. The lowest 96 hour LC_{50} of 530 µg/L was used as the starting point for estimating the chronic NOEC value for rainbow trout (steelhead), as well as input into ICE models to estimate chronic NOEC values for the remaining T&E salmonid species. The 530 µg/L short term acute value for rainbow trout was converted into a chronic NOEC by first dividing 530 µg/L by 2.27 to obtain an LC_{LOW} value of 233 µg/L. In the absence of an iodine specific acute-chronic ratio (ACR) for any species, the default national median ACR of 8.3 (Raimondo et al. 2007) was used to convert the LC_{LOW} to a chronic NOEC value of 28.1 µg/L elemental iodine.

Because no empirical toxicity data for any other T&E fish species in Washington exists for elemental iodine, we used the rainbow trout estimated chronic NOEC of 28.1 µg/L derived from the LC_{50} of 530 µg/L from Laverock et al. (1995) as input to the Interspecies Correlation Estimation (ICE) model to estimate toxicity to the other five T&E salmonids in Washington.

Output of all ICE models run with iodine for the T&E species, genera or family with available data in ICE is shown in Table PI-3. All estimated effect concentrations in Table PI-3 are acute toxicity values, not the final chronic NOEC values used in risk characterization to estimate risks to T&E fish species. Using the ICE model selection guidelines set forth in the problem formulation, models used as the basis to estimate chronic NOEC's for salmonid species are highlighted in green and bolded in Table PI-3. The remaining ICE models, with poorer predictive ability and which were not selected as the source of LC_{50}s used to estimate chronic NOEC's are shown in red in Table PI-3. As described in the problem formulation, the lower 95% confidence interval of the predicted LC_{50}, if available, is used to calculate the chronic NOEC in this BE. All ICE models used for iodine generated lower 95% confidence intervals of the LC_{50}, and are shown in this section. No information is available in ICE for any of the T&E rockfish species in Washington (bocaccio, canary rockfish, yelloweye rockfish). Therefore, elemental iodine effects on rockfish cannot be quantitatively evaluated, and must be considered as an uncertainty in this BE.

The final selected chronic NOEC values for bull trout, Chinook salmon, chum salmon, coho salmon, sockeye salmon and steelhead that were compared to the expected environmental concentration of povidone-iodine in receiving water environments are summarized in Table PI-4.

Table PI-4. Chronic no effect concentrations (NOEC) for elemental iodine

Species	Chronic NOEC (µg/L)	Source of chronic NOEC
Bull trout	25.4	ICE model – family level
Chinook salmon	23.1	ICE model – species level
Chum salmon	25.4	ICE model – family level
Coho salmon	34.3	ICE model – species level
Sockeye salmon	25.4	ICE model – family level
Steelhead	28.1	Empirical acute data (Laverock et al. 1995)

Risk Characterization: Povidone-Iodine

Risks to T&E Fish Species from Povidone-Iodine

Risks to T&E fish species for which toxic concentrations of povidone-iodine can be identified from the literature are calculated using a standard ecological risk assessment hazard quotient approach. In the hazard quotient approach, the estimated environmental concentration is divided by the chronic NOEC for each T&E species to calculate a hazard quotient. Hazard quotients less than 1.0 are indicative of acceptable levels of ecological risk. In the context of this BE, an acceptable ecological risk is represented as an EEC which, if not exceeded, results in no discernable effect on the survival, reproduction and growth of a T&E species. Note that acceptable EEC values vary between species.

Hazard quotients greater than or equal to 1.0 are indicative of a potential for unacceptable ecological risks to T&E species.

Hazard quotients for the six T&E salmonid species for which toxicity data is available or could be estimated are presented in Table PVP-HQ. Hazard quotients were calculated using the EEC generated from the lowest and highest daily discharge from the Quilcene hatchery, which results in the largest EEC range to which T&E species could be exposed.

Table PVP-HQ. Hazard quotients (HQ) for T&E species exposed to the range of estimated environmental concentrations (EEC) of povidone-iodine discharged by hatcheries.

Species	EEC range (µg/L)	Chronic NOEC (µg/L)	Hazard quotient range
Bull trout	0.0027 – 1.47	52,911	$5.1 \times 10^{-8} – 2.8 \times 10^{-5}$
Chinook salmon	0.0027 – 1.47	41,731	$6.5 \times 10^{-8} – 3.5 \times 10^{-5}$
Chum salmon	0.0027 – 1.47	52,911	$5.1 \times 10^{-8} – 2.8 \times 10^{-5}$
Coho salmon	0.0027 – 1.47	52,911	$5.1 \times 10^{-8} – 2.8 \times 10^{-5}$
Sockeye salmon	0.0027 – 1.47	52,911	$5.1 \times 10^{-8} – 2.8 \times 10^{-5}$
Steelhead	0.0027 – 1.47	100,000	$2.7 \times 10^{-8} – 1.5 \times 10^{-5}$

All hazard quotients in Table PVP-HQ are substantially lower than 1.0, indicative of acceptable levels of ecological risk to the species under all hatchery discharge scenarios. Note that the EEC values do not take into account any degradation of environmental concentrations of povidone-iodine.

Risks to Potential Prey of T&E Species from Povidone-Iodine

Limited information is available on the toxicity of povidone-iodine to other aquatic species (Appendix ???, Table ???). In addition to the empirical rainbow trout toxicity data, empirical adverse effect toxicity data for povidone-iodine exists for four algal species (Ukeles 1962), two clam species and a second fish species, largemouth bass (Wright and Snow 1975). The algal studies were run for 10 days, and can be considered chronic effect concentrations for algal species with short generation times. The clam studies (Chandler and Marking 1979, Davis and Hidu 1969) were of short duration (2 – 12 days), as was the largemouth bass study (15 minutes), and were treated as short term acute studies. Results of these studies were converted to chronic no effect concentrations using the procedures described in the problem formulation, including the results of the largemouth bass study of Wright and Snow (1975), which reported no effect on egg hatchability after a 15 minute treatment of eggs with Betadine. Chronic NOEC concentrations of povidone-iodine to prey of T&E species is summarized in Table PI-5.

Table PI-5. Toxicity of Povidone-Iodine to Prey of T&E Listed Species

Organism Type	**Chronic NOEC range (µg/L)**
Algae	50,000 – 100,000
Aquatic macrophytes	No data
Aquatic invertebrates	908 - >1,592,272
Aquatic insects	No data
Crustaceans	No data
Zooplankton	No data
Molluscs	908 - >1,592,272
Others (e.g. oligochaetes, etc.)	No data
Amphibians	No data
Fish	24,096 - >102,449

Chronic NOEC concentrations for four algal species appear comparable to those for the two fish species with empirical toxicity data for povidone-iodine. Available data for the two clam species, quahog (*Mercenaria mercenaria*) and Asiatic clam (*Corbicula manilensis*) indicates a wide range of sensitivity between these two species. The low end of the mollusc chronic NOEC range in Table PI-5 is derived from a 48 hour EC_{50} concentration of 17,100 µg/L reducing growth and development of quahog (Davis and Hidu 1969). The high end of the mollusc chronic NOEC range is derived from a 96 hour LC_{50} survival study by Chandler and Marking (1979) on the Asiatic clam *Corbicula manilensis*.

Based on the maximum EEC of 1.47 µg/L povidone-iodine, the highest hazard quotient for any prey species for which empirical PVP-I toxicity data is available is a HQ = 0.0016 for quahog, based on the results of the Davis and Hidu (1969) study. As the quahog and all other potential prey species hazard quotient for PVP-I is lower than 1.0, we conclude that povidone-iodine releases from Washington hatcheries is unlikely to adversely affect prey species of T&E fish species.

Uncertainty Analysis of Povidone-Iodine Risk Characterization

All four types of uncertainty (variation, model uncertainty, decision rule uncertainty and true unknowns) described in the problem formulation are present in this povidone-iodine evaluation. By far the largest uncertainty in this evaluation is the complete absence of toxicity data in the literature that would permit a quantitative evaluation of risks to T&E eulachon and rockfish species from povidone-iodine use at fish hatcheries. This type of uncertainty is a true unknown in this BE.

Variation of expected environmental concentrations in hatchery discharges and receiving waters is also a large source of uncertainty in this analysis. This is because the use pattern of PVP-I (disinfection of fish eggs) occurs only during a small portion of a year. The time of year during which PVP-I is potentially discharged to receiving waters varies among hatcheries, as different fish species spawn and produce eggs at different times of the year. This use pattern means that during much of the year, povidone-iodine is not released from a hatchery. Variation also is expressed in the confidence limits surrounding statistically reduced expressions of the empirical toxicity data (e.g. LC_{50}, EC_{50}, etc.). Confidence limits describe random variation around the central tendency response of laboratory organisms exposed to chemicals in toxicity tests.

Model uncertainty in the ICE models is described by the percent cross-validation success statistic. According to Raimondo et al. (2013), the percent cross-validation success rate for each model is the proportion of data points that are predicted within 5-fold of the actual LC_{50} value. There is a strong relationship between taxonomic distance and cross-validation success rate, with uncertainty generally, although not always increasing with larger taxonomic distance. Maximizing the value of the cross-validation statistic was a primary determinant of which of multiple ICE models were used to estimate toxicity values in this BE for species where no empirical toxicity data exists for a chemical-species pair.

Risk Characterization: Elemental Iodine

Risks to T&E Fish Species from Elemental Iodine

Hazard quotients for the six T&E salmonid species for which toxicity data is available or could be estimated are presented in Table I2-HQ. Hazard quotients were calculated using the EEC generated from the lowest and highest daily discharge from the Quilcene hatchery, which results in the largest EEC range to which T&E species could be exposed.

Table I2-HQ. Hazard quotients (HQ) for T&E species exposed to the range of estimated environmental concentrations (EEC) of elemental iodine discharged by hatcheries.

Species	EEC range (µg/L)	Chronic NOEC (µg/L)	Hazard quotient range
Bull trout	0.00027 – 0.147	25.4	0.000011 – 0.0058
Chinook salmon	0.00027 – 0.147	23.1	0.000012 – 0.0064
Chum salmon	0.00027 – 0.147	25.4	0.000011 – 0.0058
Coho salmon	0.00027 – 0.147	34.3	0.0000079 – 0.0043
Sockeye salmon	0.00027 – 0.147	25.4	0.000011 – 0.0058
Steelhead	0.00027 – 0.147	28.1	0.0000096 – 0.0052

All hazard quotients in Table I2-HQ are substantially lower than 1.0, indicative of acceptable levels of ecological risk to the species under all hatchery discharge scenarios. Note that the EEC values do not take into account any reduction of environmental concentrations of elemental iodine to iodide or other reduced forms.

Risks to Potential Prey of T&E Species from Elemental Iodine

Limited information is available on the toxicity of elemental iodine to other aquatic species (Appendix ???, Table ???). In addition to the empirical rainbow trout toxicity data, empirical adverse effect on survival data for iodine exists for the zooplankton species *Daphnia magna* (Laverock et al. 1995), and three fish species in addition to rainbow trout: bluegill (EPA 2013), channel catfish (LeValley 1982), and the guppy *Poecilia reticulata* (Yarzhombek et al. 1991). One no effect three day study on survival of the zebra mussel (Waller et al. 1996) exposed to iodine also exists. No chronic growth or reproductive toxicity data was found for elemental iodine for any species.

All of the available elemental iodine toxicity data are considered by EPA to be short term acute studies. All but one of the available iodine toxicity studies had exposure durations of 96 hours (4 days) or less. One rainbow trout study had an exposure duration of 14 days. As the available iodine toxicity data are all short term acute studies, their results were converted into chronic NOEC concentrations by the procedure described in the problem formulation: dividing a concentration causing acutely toxic effects on survival by 2.27 to estimate an LC_{LOW}, then dividing the LC_{LOW} by the default acute-chronic ratio of 8.3 (Raimondo et al. 2007) to estimate a chronic NOEC.

The range of chronic NOEC concentrations for potential prey species of T&E fish species in Washington is presented in Table PI-6.

Table PI-6. Toxicity of Elemental Iodine to Prey of T&E Listed Species

Organism Type	Chronic NOEC range (µg/L)
Algae	No data
Aquatic macrophytes	No data
Aquatic invertebrates	8.5 – 200,000
Aquatic insects	No data
Crustaceans	8.5
Zooplankton	8.5
Molluscs	200,000
Others (e.g. oligochaetes, etc.)	No data
Amphibians	No data
Fish	19.3 - 159

The most sensitive prey species for which empirical iodine toxicity data is available is the cladoceran *Daphnia magna*. Assuming *Daphnia* is exposed to the maximum elemental iodine EEC of 0.147 µg/L, the maximum *Daphnia* hazard quotient is 0.017. As the highest prey species hazard quotient is lower than 1.0, we have concluded that elemental iodine releases from Washington hatcheries are unlikely to adversely affect prey species of T&E fish species.

Uncertainty Analysis of Elemental Iodine Risk Characterization

All four types of uncertainty (variation, model uncertainty, decision rule uncertainty and true unknowns) described in the problem formulation are present in this elemental iodine evaluation. By far the largest uncertainty in this evaluation is the complete absence of toxicity data in the literature that would permit a quantitative evaluation of risks to T&E eulachon and rockfish species from iodine use at fish hatcheries. This type of uncertainty is a true unknown in this BE.

Variation of expected environmental concentrations in hatchery discharges and receiving waters is also a large source of uncertainty in this analysis. This is because the use pattern of elemental iodine released from PVP-I (disinfection of fish eggs) occurs only during a small portion of a year. The time of year during which iodine is potentially discharged to receiving waters varies among hatcheries, as different fish species spawn and produce eggs at different times of the year. This use pattern means that during much of the year, elemental iodine is not released from a hatchery. Variation also is expressed in the confidence limits surrounding statistically reduced expressions of the empirical toxicity data (e.g. LC_{50}, EC_{50}, etc.). Confidence limits describe random variation around the central tendency response of laboratory organisms exposed to chemicals in toxicity tests.

Model uncertainty in the ICE models is described by the percent cross-validation success statistic. According to Raimondo et al. (2013), the percent cross-validation success rate for each model is the proportion of data points that are predicted within 5-fold of the actual LC_{50} value. There is a strong relationship between taxonomic distance and cross-validation success rate, with uncertainty generally, although not always increasing with larger taxonomic distance between two species. Maximizing the value of the cross-validation statistic was a primary determinant of which of multiple ICE models were used to estimate toxicity values in this BE for species where no empirical toxicity data exists for a chemical-species pair.

Effect Determinations of Povidone-Iodine on T&E Species

Based on all chronic NOEC concentrations for six T&E salmonid species being substantially higher than the estimated environmental concentrations of povidone-iodine released from hatcheries, EPA has made the following effect determinations for povidone-iodine:

Bull trout: Not likely to adversely affect

Chinook salmon: Not likely to adversely affect

Chum salmon: Not likely to adversely affect

Coho salmon: Not likely to adversely affect

Sockeye salmon: Not likely to adversely affect

Steelhead: Not likely to adversely affect

The above determinations are all based on the estimated environmental concentrations from hatchery releases being substantially lower than the chronic NOECs for the above six species.

We are unaware of any quantitative aquatic toxicological data that would allow us to perform a quantitative ecological risk assessment on povidone-iodine risks to eulachon, bocaccio, canary rockfish, and yelloweye rockfish. This is a true unknown type of uncertainty for the hatcheries that use povidone-iodine and which also discharge into estuarine or marine waters.

Effect Determinations of Elemental Iodine on T&E Species

Based on all chronic NOEC concentrations for six T&E salmonid species being substantially higher than the estimated environmental concentrations of elemental iodine released from hatcheries, EPA has made the following effect determinations for elemental iodine:

Bull trout: Not likely to adversely affect

Chinook salmon: Not likely to adversely affect

Chum salmon: Not likely to adversely affect

Coho salmon: Not likely to adversely affect

Sockeye salmon: Not likely to adversely affect

Steelhead: Not likely to adversely affect

The above determinations are all based on the estimated environmental concentrations from hatchery releases being substantially lower than the chronic NOECs for the above six species.

As was the case for povidone-iodine, the absence of any quantitative data that allowed us to quantify risks to eulachon and the three T&E rockfish species is an uncertainty in this BE.

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